



Effects of Exercise Training and Consumption of Fenugreek Seed Extract on Expression of Oxidised LDL and ROS-related Genes in Patients with Coronary Artery Occlusion

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ABSTRACT

Background and objectives: Sedentary life style and high-fat diet are one of the key causes of coronary artery disease. The aim of this study was to evaluate effects of periodic exercise and consumption of fenugreek seed extract on the expression of oxidized low-density lipoprotein (oxLDL) and reactive oxygen species (ROS) genes in patients with coronary artery occlusion.

Methods: The present quasi-experimental study was performed on 32 men (60 ± 5 years) with coronary artery disease. The subjects were randomly divided into four groups: control, exercise, fenugreek supplementation, and combination of exercise and fenugreek supplementation. The training program consisted of eight weeks of intermittent running at 55 to 65% heart rate reserve, three sessions per week, with an emphasis on gradual overload. The subjects consumed 10 mg/kg of body weight fenugreek extract daily. Data analysis was performed using two-way analysis of variance and Tukey's test at statistical significance of 0.05.

Results: The mean expression ratio of oxLDL and ROS genes in the intervention groups decreased significantly ($p < 0.0001$). Compared with the control group, the most profound decreased in oxLDL and ROS expression occurred after combination of exercise and fenugreek supplementation ($p < 0.0001$).

Conclusion: The results showed that intermittent exercise and consumption of fenugreek seed extract might have beneficial effects on the antioxidant defense system in patients with coronary artery occlusion.

Keywords: [Exercise](#), [Fenugreek Seed](#), [Oxidised LDL](#).

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in developing countries (1,2). It is estimated that by 2020, CVD will be one of the most common diseases in the world (3). Identifying the risk factors of CVDs plays an important role in preventing sudden cardiac death. Hypertension, low-density lipoprotein (LDL) level, age, smoking, glucose intolerance, diabetes, and physical inactivity have been reported as the main causes of CVD-related mortality (4,5). Regular exercise has been regarded as an effective method of CVD prevention. Research also suggests that using herbal supplements is a good alternative to preventing cardiovascular events. The use of supplements, especially dietary supplements, has long been proposed to prevent physical weakness and improve vigor (6). The tendency of the general population to use herbal medicine has increased in recent years due to the harmful effects of chemical drugs. Fenugreek (*Trigonella foenum-graecum*) is a medicinal plant with remarkable healing properties that has long been used in Iranian traditional medicine. It has anti-atherosclerosis, anti-inflammatory as well as blood cholesterol, blood lipids, high blood pressure, and blood triglycerides lowering effects (7). On the other hand, in recent years, high-intensity intermittent exercise training (HIIT) has been recognized as an effective exercise intervention with similar or greater benefits than moderate-intensity intermittent exercise (8,9). For example, it has been reported that HIIT has similar effects to moderate-intensity intermittent exercise on skeletal muscle metabolic adaptations, cardiovascular fitness, and body composition. Both herbal supplements and physical activity are effective in controlling or preventing CVD risk factors, such as LDL level. Clinical studies have shown that the atherogenic properties of oxidized LDL-cholesterol (oxLDL-c) are greater than those of LDL-c (10-12). The mechanism of LDL-c entry into macrophages is not mediated by the LDL-c receptor (13), but several studies have shown that LDL-c, the largest carrier of cholesterol in

the blood, is first converted to oxLDL-c, and then enters macrophages by scavenger ii receptors or oxLDL-c receptors (10,11,14). It has been reported that oxLDL-c levels are very high in patients with coronary heart disease (15). Antioxidants inhibit the production of oxLDL-c (16,17). On the other hand, exercise, especially regular moderate-intensity exercise, increases the amount of antioxidants, thereby improving the body's defense system (18, 19). The Centers for Disease Control and the American College of Exercise Medicine have recommended that 30 minutes of moderate-intensity physical activity on most days of the week can improve cardiovascular health in adults (20). Increased oxidative stress and lipoprotein oxidation are associated with coronary artery disease (10). There was also a significant relationship between oxLDL-c levels and CVD-related deaths (21). Under normal conditions, about 2 to 5 percent of mitochondrial oxygen is transferred to free radical oxygen compounds such as superoxide (O_2^- , hydrogen peroxide, hydroxyl, etc.). Oxidative stress is a process caused by excess of free radicals on the surface of cell membranes, which can damage membranes of cells and intracellular organelles, especially mitochondria. Damage to lipid membranes causes cell peroxidation and lipid wall hardening. Under normal conditions, antioxidants convert reactive oxygen species (ROS) into water and prevent the production of free radicals (22, 23). The imbalance between oxidants and antioxidants disrupts the normal function of immune cells (24). High intensity physical activity, especially intense aerobic exercise, increases oxidative stress and lipid peroxidation (25). Some studies have shown that oxLDL-c had significantly reduced in patients with coronary heart disease after a period of moderate-intensity aerobic exercise along with a diet plan (26,27). The present study aimed at investigating effects of intermittent exercise and consumption of fenugreek seed extract on expression of oxLDL and ROS in patients with coronary artery occlusion.

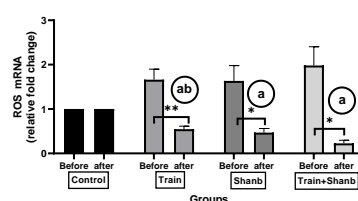


Figure 1- Comparison of mean oxLDL gene expression in different groups between the pretest and posttest stages. Before: 24 hours before interventions, After: 48 hours after the last day of interventions. Control: control group, Train: Exercise group, Shanb: Fenugreek supplementation, Shanb + Train: Exercise + Fenugreek supplementation. a: Significant difference compared to the control group ($p < 0.05$). b: significance difference compared to the fenugreek + exercise group ($p < 0.05$). *: $p < 0.05$, **: $p < 0.0001$.

RESULTS

The mean level of oxLDL gene expression decreased significantly after the training, fenugreek supplementation, and combination of fenugreek supplementation with training ($p<0.0001$). The results of Tukey's post hoc test also showed that the mean level of oxLDL gene expression differed significantly between

the intervention and control groups ($p<0.0001$) (Figure 1). The mean level of ROS expression decreased significantly in all intervention groups ($p<0.0001$). Moreover, the mean level of ROS expression in the posttest stage was significantly lower in all intervention groups compared with the control group ($p<0.0001$).



Figure 2- Comparison of mean ROS gene expression in different groups between the pretest and posttest stages. a: Significant difference compared to the control group ($p<0.05$). b: significance difference compared to the fenugreek + exercise group ($p<0.05$). *: $p<0.05$, **: $p<0.0001$

DISCUSSION

Due to sociocultural modernization and decrease in physical activity, the incidence of diseases caused by physical inactivity, such as CVD, is on the rise increasing (1,2). The present study evaluated the effects of intermittent exercise and fenugreek seed extract supplementation on expression of oxLDL and ROS in patients with coronary artery occlusion. Based on the results, the expression of ROS and oxLDL genes reduced significantly after the intervention. A previous study also reported that oxLDL-c levels reduced significantly in patients with coronary heart disease after a period of moderate-intensity aerobic exercise with a diet plan (28). Under normal conditions, there is a balance between the amount of ROS and antioxidants (29). Disruption of this balance and the increase in ROS, especially during strenuous exercise, causes oxidative stress (25). During intense endurance (aerobic) training, the production of ROS increases, mainly in the mitochondria of active muscle cells (30). It has been shown that fenugreek has anti-atherosclerotic, anti-inflammatory, and antioxidant effects (31). Interval training may lead to overproduction of free radicals (32,33). Some studies on both animals and humans have reported an increase in free radicals production after aerobic or anaerobic training in subjects with coronary artery disease (32,34). The binding of oxLDL to low-density lipoprotein receptor-1 (LOX-1) activates NADPH oxidase by inducing translocation of specific subunits on the cell membrane,

leading to a rapid elevation in intracellular ROS, such as hydrogen peroxide and superoxide; the latter decreases intracellular nitric oxide and upregulates LOX-1 expression, thus resulting in further increase in ROS production (33-35).

Flavonoids can regulate some steps of angiogenesis, such as cell migration and the formation of microcapillary tubules (35). It has been demonstrated that fenugreek could improve maximal and submaximal aerobic function (34). In addition, fenugreek extract can significantly reduce the atherogenic index. Fenugreek contains bitter saponins such as protodioscin. Studies have shown the effect of diazine (a form of protodioscin and diosin) on fat and glucose metabolism. Diosgenin increases the amount of PPAR- γ in white adipose tissue and induces the differentiation of fat cells and reduces the size of adipocytes. This increases the secretion of adiponectin, which inhibits inflammation in adipocytes (33). In this study, control of each subject's diet, level of motivation, mental stress, lifestyle, endocrine secretion, as well as genetic and congenital characteristics could not be controlled.

The limitations of the present study were the small number of subjects and the measurement of limited angiogenic indices. Therefore, it is suggested to conduct future studies on larger study populations in order to understand the possible effects of periodic exercises and fenugreek extract supplementation.

CONCLUSION

Interval training may lead to adaptations faster than continuous aerobic training. The results of this research showed that a combination of interval training and fenugreek seed extract supplementation can reduce oxLDL and expression of ROS-related genes. Therefore, the use of this supplement could have beneficial effects on antioxidant defense of patients with coronary artery occlusion.

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DECLARATIONS

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Ethics approvals and consent to participate

Written consent was taken from all subjects prior to participation in the study. The study has been approved by the Ethics Committee of the Islamic Azad University, Babol Branch, Iran (ethical approval code: IR.IAU.BABOL.REC.1398.091).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding publication of this article.

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